



US005175144A

United States Patent [19]

Walser

[11] **Patent Number:** **5,175,144**[45] **Date of Patent:** **Dec. 29, 1992****[54] METHOD OF RETARDING THE PROGRESSION OF CHRONIC RENAL FAILURE**[75] Inventor: **Mackenzie Walser, Ruxton, Md.**[73] Assignee: **The Johns Hopkins University, Baltimore, Md.**[21] Appl. No.: **277,161**[22] Filed **Nov. 29, 1988**[51] Int. Cl.⁵ **A61K 37/00; A61K 31/56; A61K 21/495; A61K 31/50; A61K 31/44; A61K 31/445**[52] U.S. Cl. **514/2; 514/11; 514/179; 514/252; 514/282; 514/289; 514/327**[58] Field of Search **514/179, 2, 11, 252, 514/282, 289, 327****[56] References Cited****U.S. PATENT DOCUMENTS**3,714,159 1/1973 Janssen et al. 424/601
4,320,146 3/1982 Walser 424/601**OTHER PUBLICATIONS**The Merck Manual (14th edition, 1982) pp. 2388-2389.
Avery's Drug Treatment, 3rd edition (1987) pp. 897-898.
W. E. Mitch, et al., "The Effect of Keto Acid-Acid Supplement to Restricted Diet on the Progression of Chronic Renal Failure", *The New England Journal of Medicine*, 311:623-629 (Sep. 6), 1984.J. Burns, et al., "Comparison of the effects of keto acid analogues and essential amino acids on nitrogen homeostasis in uremic patients on moderately protein-restricted diets", *The American Journal of Clinical Nutrition* 31: Oct. 1978, pp. 1767-1775.M. Walser, et al., "Progression of chronic renal failure in patients given ketoacids following amino acids", *Kidney International*, vol. 32 (1987), pp. 123-128.N. Gretz, et al., "Low-proteindiet supplemented by keto acids in chronic renal failure: A prospective controlled study", *Kidney International*, vol. 24, Suppl. 16 (1983), pp. S-263-S-267.

G. Barsotti, et al., "Effects on Renal Function of a Low-Nitrogen Diet Supplemented with Essential Amino Acids and Ketoanalogues and of Hemodialysis

and Free Protein Supply in Patients with Chronic Renal Failure", *Nephron* 27:113-117 (1981).T. Taylor, et al., "B-Endorphin Suppresses Adrenocorticotropin and Cortisol Levels in Normal Human Subjects", *Journal of Clinical Endocrinology and Metabolism*, vol. 57, No. 3, pp. 592-596 (1983).B. Ambrosi, et al., "Loperamide, an Opiate Analogue, Inhibits Plasma Acth Levels in Patients with Addison's Disease", *Clinical endocrinology*, 24, pp. 483-489 (1986).G. Teutsch, et al., "17a-Alkynyl-11b,17-Dihydroxyandrostane Derivatives: A New Class of Potent Glucocorticoids.", *Steroids*, vol. 38, No. 6, pp. 651-665 (1981).M. Moguilewsky, et al., "RU 38486: Potent Antigluco-corticoid Activity Correlated with Strong Binding to the Cytosolic Glucocorticoid Receptor Followed by an Impaired Activation", *S. Steroid Biochem*, vol. 20, No. 1, pp. 271-276 (1984).Roland M. Schaefer, et al., "Evidence for Reduced Catabolism by the Antigluco-corticoid RU 38486 in Acutely Uremic Rats", *Am. J. Nephrol*, 7, pp. 127-131 (1987).Xavier Bertagna, et al., "The New Steroid Analog RU 486 Inhibits Glucocorticoid Action in Man", *Journal of Clinical Endocrinology and Metabolism*, vol. 59, No. 1, pp. 25-28 (1984).

(List continued on next page.)

Primary Examiner—Frederick E. Waddell*Assistant Examiner*—Raymond J. Henley, III*Attorney, Agent, or Firm*—Panitch Schwarze Jacobs & Nadel

[57]

ABSTRACT

Progression of chronic renal failure can be retarded (slowed or arrested) by administering to humans suffering from such disorder an agent which suppresses the production of glucocorticoids in the human. The agents may be administered alone or in combination with a protein restricted and/or phosphorus restricted diet. Examples of suitable agents which either suppress production of glucocorticoids or block binding to their receptors include sodium valproate, enkephalins, opioids, clonidine, ketoconazole, oxytocin, and mifepristone.

10 Claims, 1 Drawing Sheet